Nasal decongestive compositions

GB Patent # GB1087842

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Inventor(s)
HOEGBERG KNUT BERTIL
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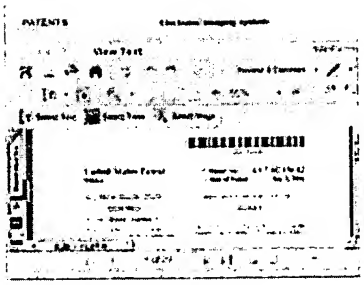
Abstract

Abstract of GB1087842 Aerosol compositions, for use as nasal decongestants, comprise polypl hydrochloride as active ingredients, together with eucalyptol, and dipropylene glycol, with 1,2 - (propellant. Other analogues of polyphloretin phosphate may be used (see Divisions A5-A6).ALS administration comprise a non-toxic carrier with 0.02% to 2.0% by weight of an anti-enzymatic c which is a condensation product of phosphoric acid with one or more of mono-, di-, or poly-nucl reactive groups in the meta-or para-position to each other in the same nucleus or di- or polynuc two different reactive groups being -OH, -SH, or -NH3 groups, the linkage to the phosphoric aci the reactive groups, the condensation products containing free -OH groups attached to the phos alkaline pH. Particular such compounds are the following phosphates: polyphloretin, polymethyl polyhesperidin, and polyphloroglucinol phosphate. The compositions may take the form of an ac propelled aerosol composition (see Div. C4-C5), and may contain other active ingredients such antihistamines. Sympathominetic amines used may be phenylephrine, methoxamine, cyclopent xylometazoline, hydroxy amphetamine cyclopentamine, mephentermine, methylhexaneamine, a specified are amphomycin, bacitracin, erythromycin, chloramphenicol, neomycin, polymixin tetra

Title Information



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1 **No title available**
Inventor: **Applicant:** (BR)
EC: A61K31/66; A61K31/665; (+2) **IPC:** ***A61K31/66; A61K31/665; A61K31/7***
Publication info: BE647337 A - 1964-10-30

2 **No title available**
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Publication info: FR3690M M - 0000-00-00

3 **Nasal decongestive compositions**
Inventor: HOEGBERG KNUT BERTIL; FERNOE OVE BIRGER; (+1) **Applicant:** LEO AB (BR)
EC: A61K31/66; A61K31/665; (+2) **IPC:** ***A61K31/66; A61K31/665; A61K31/7***
Publication info: GB1087842 A - 1967-10-18

4 **Decongestive compositions and method**
Inventor: BIRGER FERNO OVE; BERTIL HOGBERG KNUT; (+1) **Applicant:** LEO AB (BR)
EC: A61K31/66; A61K31/665; (+2) **IPC:** ***A61K31/66; A61K31/665; A61K31/7***

Publication info: US3317383 A - 1967-05-02

List of citing documents

1 **METHOD AND COMPOSITION FOR TREATMENT OF SKIN CONDITIONS**
Inventor: HUTTERER JEFFREY (US) **Applicant:** HUTTERER JEFFREY (US) (BR)
EC: **IPC:** ***A61K31/137; A61K31/55; A61K31/573(+***
Publication info: WO2005097139 - 2005-10-20

2 **Pharmaceutical composition for treatment of rhinitis**
Inventor: GREVE HARALD DR (DE); GREVE RAINER DR (DE) **Applicant:** KLOSTERFRAU MCM VETRIEB G
EC: A61K31/137; A61K31/4174; (+2) **IPC:** ***A61K45/00; A61K9/00; A61K31/137(+28***
Publication info: EP1532986 - 2005-05-25

Claims

WHAT WE CLAIM IS:-

1. A nasal decongestive composition for topical administration comprising:

(a) as the effective nasal decongestive ingredient 0.02% to 2.0% by weight of an antienzymatic organic compound ha and which is a condensation product of phosphoric acid with one or more of the following aromatic compounds:

(1) mono-, di- or polynuclear aromatic compounds containing at least two reactive groups in the meta-position to each polynuclear aromatic compounds containing at least two reactive groups in the para-position to each other in the sam compounds containing at least two different reactive groups on different nuclei, the said reactive groups being -OH, -S groups of the phosphoric acid being through the polyvalent atoms of the said reactive groups, the said condensation p the phosphorus atoms of the phosphoric acid groups and being soluble in water at alkaline pH, and (b) a non-toxic ph

2. A composition according to claim 1, in which the antienzymatic organic compound is present in an amount of 0.05 t

3. A composition according to either one of claims 1 or 2, in which the anti-enzymatic compound is polyphloretin phos

4. A composition according to either one of claims 1. or 2, in which the anti-enzymatic compound is polyphloroglucino

5. A composition according to either one of claims 1 or 2, in which the anti-enzymatic compound is polyquercetin phos

6. A composition according to either one of claims 1 or 2, in which the anti-enzymatic compound is polyhesperidin phc

7. A composition according to any one of the preceding claims which also includes 0.1 to 0.5% by weight of a sympat

8. A composition according to claim 7, in which the sympathomimetic amine is phenylephrine.

9. A nasal decongestive composition for topical administration according to claim 1 0,500 6,750 0,100 0,100 0,020 0,(as hereinbefore described with reference to the Examples.

STEVENS, LANGNER, PARRY & ROLLINSON, Chartered Patent Agents, Agents for the Applicants.

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-1967. Published by The Patent Office, 25 Southampton Buildings, London, W.C.2, from which copies may be obtaine

Description

PATENT SPECIFICATION

NO DRAWINGS Inventors: KNUT BERTIL HOGBERG, OVE] TORSTEN OVE ENOK LINDEROT Date of filing Comp

Application Date: May 1, 1963.

Complete Specification Published: Oct. 18. 1967.

. -,.:42 ,. 1 i 11,087.842 BIRGER FERNo and No. 17242/63.

Index at acceptance:-A5 B(1D, IE, IF, 1G, 1H, IM, 1R2, IS); C4 X11 Int. 01.:-A 61 k 3/54 ERRATA SPECIFICATION N

Page 3, line 19, for "are" read "as" Page 6, Example 5, first line, for "polyphloretin" read "Polyphloretin" Page 6, Exam "saccharin" Page 8, Example 9, first line, for "polyphloroglucinol" read "Polyphloroglucinol" Page 9, Example 11, first l Page 9, Example 11, second line, for "6,750" read "7,650" THE PATENT OFFICE 20th November 1967 nas knc..-- - l sympathomimetic amine. Compounds of the hydrocortisone group show, however, disagreeable side-effects in the re mechanism of the tissue against infection. Further the duration of the anti-rhinitic effect of such compositions is rather the beneficial effects of formerly known decongestive preparations but without their disadvantageous side-effect has l surprisingly shown that certain high-molecular weight, antienzymatic compounds show a decongestive effect on the n give rise to the undesirable side-effects mentioned above. The decongestive effect is even superior to that obtained w

In addition the compositions containing these compounds show a protracted effect superior to previously known comp toxic, especially when administered topically and to nasal mucosa.

[Price 4s. 6d.] ion Imrisinltilemd ric ing mTive her imive her in the same nucleus, or (3) di- or polynuclear aromatic cor groups on different nuclei, the said reactive groups being -OH, -SH or -NH, groups and the linking to the acid groups (polyvalent atoms of the said reactive groups, the said condensation products containing free hydroxy groups linked tc groups and being soluble in water at alkaline pH, and (b) a non-toxic pharmaceutically acceptable carrier therefor.

The high molecular weight anti-enzymatic compound used in the composition of the present invention has a molecula the preferred molecular weight being 2,000 to 25,000.

To further enhance the therapeutic effect 0.1 to 0.5% by weight of a sympathomimetic amine may be present in the c also be included.

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anc dec rhii sidc for (PATENT SPECIFICATION

Nq hi NO DRAWINGS Inventors: KNUT BERTIL HOGBERG, OVE n - = TORSTEN OVE ENOK LINDEROT I Be i Dat 1964.

0 PA be Application Date: May 1, 1963. 1 P.; 2 3 w Complete Specification Published: Oct. 18, 1967.

1,087,842 BIRGER FERN6 and No. 17242/63.

Index at acceptance:-A5 B(1D, 1E, iF, 1G, 1H, IM, 1R2, IS); C4 X11 Int. CL.:-.A 61 k 3/54 COMPLETE SPECIFICATI

Nasal Decongestive Compositions We, AKTIEBOLAGET LEO, a Body Corporate organized under the laws of Swede Sweden, do hereby declare the invention, for which we pray that a Patent may be granted to us, and the method by w described in and by the following statement: -

This invention relates to a medicinal composition having particular utility for the treatment of rhinitis. The composition degree of decongestive action on nasal mucosas with rhinitic disorders without showing any serious side-effects. The therapeutic effect.

Compositions with a decongestive effect on nasal mucosas with rhinitic disorders are wellknown in the art, e.g. hydro a sympathomimetic amine. Compounds of the hydrocortisone group show, however, disagreeable side-effects in the mechanism of the tissue against infection. Further the duration of the anti-rhinitic effect of such compositions is rather the beneficial effects of formerly known decongestive preparations but without their disadvantageous side-effect has l surprisingly shown that certain high-molecular weight, antienzymatic compounds show a decongestive effect on the n give rise to the undesirable side-effects mentioned above. The decongestive effect is even superior to that obtained w

In addition the compositions containing these compounds show a protracted effect superior to previously known comp toxic, especially when administered topically and to nasal mucosa.

[Price 4s. 6d.] In accordance with the present invention there is provided a nasal decongestive composition for topical

(a) as the effective nasal decongestive ingredient 0.02()2 to 2.0% by weight of antienzymatic organic compound havir and which is a condensation product of phosphoric acid with one or more of the following aromatic compounds:

(1) mono-, di- or polynuclear aromatic compounds containing at least two reactive groups in the meta-position to eacl polynuclear aromatic compounds containing at least two reactive groups in the para-position to each other in the sam compounds containing at least two different reactive groups on different nuclei, the said reactive groups being -OH, -S groups of the phosphoric acid being through the polyvalent atoms of the said reactive groups, the said condensation p the phosphorus atoms of the phosphoric acid groups and being soluble in water at alkaline pH, and (b) a non-toxic ph

The high molecular weight anti-enzymatic compound used in the composition of the present invention has a molecula the preferred molecular weight being 2,000 to 25,000.

To further enhance the therapeutic effect 0.1 to 0.5%/O by weight of a sympathomimetic amine may be present in the also be included.

By the term "sympathomimetic amine" is meant the amine itself as well as pharmaceutically acceptable salts thereof. the form of a pharmaceutically acceptable organic or inorganic salt, such as the hydrochloride, hydrobromide, phosph methanesulfonate, ethanesulfonate, lactate, citrate, tartrate, maleate or pamoate.

Other acid addition salts are equally suitable and may be employed if desired. As examples of sympathomimetic amir methoxamine, cyclopentadrine, naphazoline, tetrahydrozoline, xylometazoline ("Otrivin"), hydroxyamphetamine, cyclo methylhexaneamine and phenylpropylmethylamine and especially phenylephrine. The word "Otrivin" is a registered T

As examples of antibiotics that are useful in the present invention can be mentioned amphomycin, bacitracin, erythror tetracyclins and tyrothricin. Also other pharmacologically active ingredients such as antihistamines may be added witl invention.

A more detailed description of the production of the high molecular weight, antienzymatic organic compounds used in invention is given in our British specifications Nos.

700,761, 753,319 and 757,800. They have been recognized as effective antienzymatic agents, e.g. anti-hyaluronidas exploited in prolonging the activity of ACTH compositions. Certain of these active agents have also been suggested f as in the treatment of bums, or in the treatment of peritonitis, in which cases it has been thought to exert an effect upc injected locally. However, to the best of our knowledge, none of these active ingredients have been previously sugge or for any method involving application to nasal mucosa or otherwise for use in connection with any rhinitic disorder.

Particularly useful for the composition of this invention are the polymers, the monomer of which is a polyhydroxybenz and the polymers: polyphloretin phosphate, polymethylphloretin phosphate, polyquercetin phosphate, polynaringenin the glucosides of these.

Even more particularly useful are polyhesperidin phosphate, polyphloretin phosphate, polyquercetin phosphate and p

The compositions of this invention may be used for the topical treatment of manifestations of rhinitic disorders of the r from 0.02 to two milligrams, preferably 0.05 to one milligram, of a high molecular weight, antienzymatic organic comp with 0.1 to 0.5 milligrams of a sympathomimetic amine, together with a non-toxic pharmaceutical carrier or diluent.

Preparations of polyphloretin phosphate alone and polyphloretin phosphate plus sympathomimetic amines have been objective method of registration. The resistance of a standardized stream of air through the nasal passages was mea patients each and the effect was checked by inspection of the mucuous membranes and by interviewing the patients.

1,087,842 Results:

Decongestive action Protracted Preparation Very good Good Slight effect >2 hours in no of cases no of cases A. Poly Hydroxyamphetamine HBr 0,5% -+ phenylephrine HCl 0,125%, in water C. A+B D. Polyphloretin phosphate, 0,2% + p Hydrocortisone 0,02% + B, in water As can be seen, A produced a considerably better decongestive action than B an effect of the sympathomimetic amines is also clearly indicated in C when compared to A and B. An additional effect o phosphate was that the tenacious secretions became more fluid, an effect that is considered a therapeutic advantage

The above-mentioned favourable effects of polyphloretin phosphate have also been clinically confirmed in 300 outpat

Because of the non-absorbability of the high-molecular weight, antienzymetic compound, no side effects are likely to

Nor have any such side effects been reported in clinical trials.-Similar results are reported above have been obtained phosphate and polyhesperidin phosphate.

The compositions of this invention may be in the form of a solution, preferably an aqueous solution, or a selfpropelled vehicles are isotonic saline solutions, isotonic dextrose solutions, isotonic buffer solutions and propellants such as low For maximum stability of the high molecular weight, antienzymatic compound, the preparation should desirably have a

The selected high molecular weight, antienzymatic compound is present in the composition of this invention in an amo preparation and advantageously from 0.05% to 1.0% by weight of the preparation. The sympathomimetic amines and 0.5% by weight.

The following examples are given by way of illustration of composition of the invention.

1,087,842 1,087,842 EXAMPLE 1

Polyphloretin phosphate, sodium salt Glycerol Ethylenediaminetetraacetic acid, disodium salt Sodium citrate Sacchar basic Ethyl alcohol Water q.s. to make total volume of The basic phenylmercuric nitrate is dissolved in water with the .

The ethylenediaminetetraacetic acid disodium salt, sodium citrate and the saccharin sodium are dissolved while cooli sodium salt is added per cent w/v 0,100 7,650 0,100 0,100 0,020 0,009 0,001 0,900 cc with stirring. The eucalyptol di the glycerol. The thus mixed ingredients are then 10 filtered and sufficient water added to make the total volume equa

EXAMPLE 2

Polyphloretin phosphate, sodium salt Phenylephrine HCl Glycerol Ethylenediaminetetraacetic acid, disodium salt Sod Phenylmercuric nitrate, basic Ethyl alcohol Water q.s. to make total volume of per cent w/v 0,200 0,250 7,650 0,100 0 set forth in Example 1 is followed. The phenylephrine just before the eucalyptol.

HCl is added 1,087,842 EXAMPLE 3

Polyphloretin phosphate, sodium salt Phenylephrine tartrate Glycerol Ethylenediaminetetraacetic acid, disodium salt I Cyclamate sodium Eucalyptol Phenylmercuric nitrate, basic Ethyl alcohol Water q.s. to make total volume of per cent 0,001 0,900 cc The procedure set forth in Example 2 is sodium is added together with the saccharin 5 followed, the s

by disodium phosphate 2 H,0. The cyclamate EXAMPLE 4

Polyphloretin phosphate, sodium salt Phenylephrine maleate Sorbitol Ethylenediaminetetraacetic acid, disodium salt I Menthol Thimerosal N.F.

Ethyl alcohol The procedure set forth in Example 2 is mercuric nit.

followed, the sodium citrate being replaced lyptol by m(by potassium phthalate, the basic phenylper cent w/v 1,000 0 rate by thimerosal and the eucamnthol.

1,087,842 EXAMPLE 5 polyphloretin phosphate, sodium salt Phenylephrine HCl Ethylenediaminetetraacetic acid, dis Eucalyptol Phenylmercuric nitrate, basic Ethyl alcohol Water q.s. to make total volume of per cent wlv 0,500 0,250 0,1 procedure set forth in Example 2 is followed, the sodium citrate being replaced by dextrose and the glycerol being om

EXAMPLE 6

Polyphloretin phosphate, sodium salt Phenylephrine HCl Sorbitol Ethylenediaminetetraacetic acid, disodium salt Sodi Phenylmercuric nitrate, basic Polyoxyethylene sorbitan monolaurate ("Tween" 20, Atlas) Water q.s. to make total volu Mark.

per cent w/v 0,200 0,250 7,650 0,100 0,040 0,020 0,009 0,001 0,090 cc The procedure set forth in Example 2 is bitol, the glycerol being replaced by sor- and the ethyl alcohol by "Tween" 20.

6 1,087,842 EXAMPLE 7

Polyphloretin phosphate Phenylephrine HC1 Eucalyptol Dipropyleneglycol 1,2-Dichloro-1,1,2,2, tetrafluoroethane ("Fr "Freon" is a Registered Trade Mark.

The phenylephrine HC1 and the eucalyptol are dissolved in the dipropyleneglycol, the polyphloretinphosphate is pulv 20,000 cc persed in the solution. This mixture is then 5 added to the "Freon" 114, which is kept at - 250 C, and mixed

EXAMPLE 8

Polyphloretin phosphate, sodium salt Phenylephrine HGI Hydroxy-amphetamine HBr Glycerol Ethylenediaminetetraa Saccharin sodium Eucalyptol Phenylmercuric nitrate, basic Ethyl alcohol Water q.s. to make total volume of per cent v

0,009 0,001 0,900 cc The procedure set forth in Example 2 is followed. The hydroxyamphetamine HBr is added toget

1,087,842 EXAMPLE 9 polyphloroglucinol phosphate, sodium salt Glycerol Ethylenediaminetetraacetic acid, disodiun Eucalyptol Phenylmercuric nitrate, basic Ethyl alcohol Water q.s. to make total volume of The procedure set forth in E

per cent w/v 0,100 7,650 0,100 0,100 0,020 0,009 0,001 0,900 cc EXAMPLE 10

Polyquercetin phosphate, sodium salt Glycerol Ethylenediaminetetraacetic acid, disodium salt Sodium citrate Sacchai basic Ethyl alcohol Water q.s. to make total volume of The procedure set forth in Example 1 is followed.

per cent w/v 0,300 7,650 0,100 0,100 0,020 0,009 0,001 0,900 cc 1,087,842 EXAMPLE 1 1 per cent w/v Polyesperidi Ethylenediaminetetraacetic acid, disodium salt Sodium citrate Saccharin sodium Eucalyptol Phenylmercuric nitrate, b: volume of The procedure set forth in Example 1 is followed.

The high order of activity of the active agents of the present invention and compositions thereof, as evidenced by test on their valuable activity in lower animals as well as in human beings. Clinical evaluation in human beings has not yet

It will be clearly understood that the distribution and marketing of any compound or composition falling within the scop beings will of course have to be predicated upon prior approval by governmental agencies, such as the General Medi authorized to pass judgment on such questions.

Previous Patent (Developments in or relating to bedpans) Next Patent (Improvements in or relating to the grinding o...)